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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/768,442	01/24/2001	Chun-Ying Huang	U 012951-1	2379

7590

12/30/2005

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EXAMINER

JONES, DAMERON LEVEST

ART UNIT	PAPER NUMBER
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1618

DATE MAILED: 12/30/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/768,442

Applicant(s)

HUANG ET AL.

Examiner

D. L. Jones

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 9/19/05; 1/27/05; & 7/25/05.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 9 and 11 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 9 and 11 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☒ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>1/27/05</u> . | 6) <input type="checkbox"/> Other: _____ |

ACKNOWLEDGMENTS

1. The Examiner acknowledges receipt of the amendment filed 7/25/05 wherein claim s 1-8 and 10 are canceled and claim 9 is amended. In addition, the acceptable RCE (Request for Continued Examination) filed 9/19/05 is acknowledged.

Note: Claims 9 and 11 are pending.

RESPONSE TO APPLICANT'S AMENDMENT/ARGUMENTS

2. The Applicant's arguments filed 7/25/05 to the rejection of claims 9 and 11 made by the Examiner under 35 USC 102 and/or 103 have been fully considered and deemed non-persuasive for reasons of record below and those set forth in the office actions mailed 5/24/04 and 11/21/02.

102 Rejection

The rejection of claims 9 and 112 under 35 USC 102 (a,e) as being anticipated by Lentz (US Patent No. 6,231,536) is MAINTAINED for reasons of record.

Applicant asserts that the instant invention is distinguished over Lentz because Applicant has limited the term 'comprising' of claim 9 to 'consisting of' so that the claimed method merely includes administration of thalidomide.

First, amended independent claim 9 reads 'A method for treating hepatocellular carcinoma **comprising**.... Thus, the method steps are not limited to administering only thalidomide. Secondly, the phrase 'composition consisting of thalidomide' does not distinguish the instant invention over the cited prior art because in the cited prior art (column 8, Example 4), thalidomide is administered alone to the subject. Hence, since

the ultrapheresis step was done prior to the administering of thalidomide, the limitations of Applicant's claims are met.

103 Rejection

The rejection of claims 9 and 11 under 35 USC 103(a) as being unpatentable over D'Amato (US Patent No. 5,629,327) and Masiero (Angiogenesis, 1997, Vol. 1, No. 1, pages 23-35) and Patierno (US Patent No. 5,696,092) is MAINTAINED for reasons of record.

Applicant asserts that one of ordinary skill in the art would not have a reasonable expectation of success based on the cited references for treating hepatocellular carcinoma.

As set forth in the previous office actions, a skilled practitioner in the art would be to combine the references because D'Amato generally discloses treating solid tumors (cancers) that are associated with angiogenesis using thalidomide. In addition, the reference provides a disclosure that thalidomide may be used to treat various cancers that have angiogenic behavior (e.g. that thalidomide is an anti-angiogenesis agent). The Masiero reference disclose that thalidomide is used to treat prostate and breast cancer. The Patierno reference disclose that liver cancers are specifically treatable with anti-angiogenesis agents and that such cancers 4respon in a similar fashion to such agents as compared to prostate cancer, etc (see columns 8-9). As a result, one of ordinary skill in the art would be motivated to employ the thalidomide disclosed as an anti-angiogenesis agent by D'Amato as and anti-cancer agent by Masiero in various

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related cancers because it is known in the art that liver cancers (e.g., hepatocellular carcinoma) respond well to such anti-angiogenesis agents; hence, providing a useful treatment for such cancers with a reasonable expectation of success. As a result, one of ordinary skill in the art would have been motivated to use the anti-angiogenesis agent thalidomide as disclosed by D'Amato to its fullest potential to treat any cancers that respond to such agents.

NEW GROUNDS OF REJECTIONS

103 Rejection

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

4. Claims 9 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Aarestrup et al (Brazilian Journal of Medical and Biological Research, 1995, Vol. 28, pages 1069-1076).

Aarestrup et al disclose the effect of thalidomide on granulomas in mice. Subjects were administered 30 mg/kg body weight of thalidomide daily for 14, 21, or 28 day. The administration of thalidomide resulted in the reduction of the size and total number of liver granulomas (see entire document, especially, abstract; page 1069, 'Introduction'; page 1070, column 1-2, bridging paragraph; page 1071, 'Results' page

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1072, Figure 1; page 1074, columns 1-2, bridging paragraph). Aarestrup et al fail to disclose that the granuloma in the liver is malignant (cancerous).

Lentz discloses a method of treating hepatocellular carcinoma (liver metastases) comprising administering a thalidomide pharmaceutical composition (column 8, Example 4). The dosage of thalidomide is 200 mg (column 8, Example 4) which is within the scope of the claimed dosage range.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the teachings of Aarestrup et al using the teachings of Lentz (US Patent No. 6,231,536) and administer thalidomide for treating malignant granuloma of the liver because Aarestrup et al disclose the use of thalidomide alone for treating granulomas and Lentz discloses that thalidomide is useful in the treatment of hepatocellular carcinoma. Thus, a skilled practitioner in the art would recognize that if thalidomide alone is useful in the treatment of granulomas of the liver and Lentz discloses that thalidomide is successful in reducing liver tumors, a skilled practitioner would be motivated to use thalidomide alone as in Aarestrup et al for treatment of hepatocellular carcinoma (i.e., malignant granulomas). Furthermore, it is noted that Aarestrup et al disclose that the number and size of granulomas in the liver resulted in the reduction of liver granulomas; thus, further motivating one to use it alone in the treatment of hepatocellular carcinomas.

PRIORITY DOCUMENT

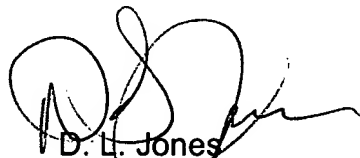
5. *Applicant is once again reminded that the priority documents are not of record.*

Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Taiwan on 2/2/2000. It is noted, however, that applicant has not filed a certified copy of the 89101826 application as required by 35 U.S.C. 119(b).

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to D. L. Jones whose telephone number is (571) 272-0617. The examiner can normally be reached on Mon.-Fri., 6:45 a.m. - 3:15 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


D. L. Jones
Primary Examiner
Art Unit 1618

December 23, 2005